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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/044,848	01/11/2002	Ram Dutta Pathak	P30835DIV2C2	9105

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EXAMINER	
PULLIAM, AMY E	

ART UNIT	PAPER NUMBER
1615	25

DATE MAILED: 12/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/044,848	Applicant(s) PATHAK ET AL.	
	Examiner Amy E Pulliam	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt of Papers

Receipt is acknowledged of the Request for Extension of Time, the Request for Continued Examination, and the Amendment D, all received by the Office July 10, 2003, as well as the Supplemental Amendment E, received by the Office September 16, 2003.

Status of Claims

Claims 2-and 21 are amended, and claims 20-33 are currently pending.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 20-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 92/09281 to Johnson alone, OR in view of Remington's Pharmaceutical Sciences, either the Fifteenth Edition or the Seventeenth Edition.

Johnson discloses the use of paroxetine or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for use in the treatment of senile dementia (abstract). Johnson further teaches that an acceptable salt of paroxetine is paroxetine hydrochloride (p 1, l 34-35). Johnson also teaches that the medicament can be in tablet form for oral administration (p 2, l 29), and may include excipients suitable for oral administration, such as calcium phosphate, magnesium stearate, and sodium starch glycolate (p 3, l 1-8). Johnson also teaches that the formulation will generally contain between 2 and 1000 mg, more preferably between 30 and 500 mg per dosage form (p 4, l 32-35). Lastly, Johnson teaches that the formulation may be obtained by conventional methods of blending, filling, tabletting, or the like (p 3, l 12-13). Specifically, in example 1, Johnson teaches that the components of the composition were mixed together in a conventional manner and compressed into a tablet in a conventional manner. Neither water nor a solvent are mentioned in the listing of ingredients in example 1 of the reference.

Johnson does not *specifically* teach that the formulation is made through dry mixing.

However, Johnson is interpreted as suggesting dry mixing. As discussed above, Johnson provides an example on page, which teaches that the components of the formulation, including the active and excipients, were mixed together. The example is detailed, in that it describes details down to including the 3 mg of lubricant. However, there is no mention of water, in either the example, or in the specification, in reference to the process of making the formulation. Based on these teachings, it is the position of the examiner that one skilled in the art would have

used dry mixing to create the formulation. The expected result would be a successful formulation, useful in treating a patient for dementia, , bulimia, migraine, or anorexia, as discussed by Johnson.

Additionally, Johnson can be taken in view of Remington's. Both the Fifteenth Edition and the Seventeenth Edition of Remington's Pharmaceutical Sciences, published in 1975 and 1990, respectively, teach that there are three known processes for making tablets- wet granulation, dry granulation and direct compression. Remington's teaches that there are reasons for choosing one method over another, for instance, wet granulation has a greater number of steps required, as well as increased time and labor. Additionally, wet granulation is unsuccessful with actives which are sensitive to moisture or temperature. On the other hand, dry granulation is useful with actives which are sensitive to moisture and which have sufficient inherent binding or cohesive properties.

It is the position of the examiner that one of ordinary skill in the art would have been motivated to combined the teachings of the above two references. First, Johnson teaches that the formulation may be made by any conventional method known in the art. Second, the example of Johnson does not teach the presence of water, or a different solvent, and instead teaches mixing the components listed in any conventional manner. One skilled in the art would look to a well known pharmaceutical guidebook, such as Remington's, to determine what "conventional methods" entail. As stated above, Remington's teaches three known methods: wet granulation, dry granulation, and direct compression. Therefore, absent evidence to the contrary, one skilled in the art would have been motivated to use any of these well known methods to make the formulation disclosed by Johnson. Furthermore, it would have been obvious to chose the method

which would allow the producer to obtain the best possible product, in both appearance and function. The expected result would be a successful pharmaceutical formulation successful in the treatment of a patient suffering from dementia, anorexia, bulimia, or migraines, as discussed by Johnson.

Therefore, whether suggested by Johnson alone, or by Johnson in view of Remington's, this invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Applicants' Arguments

Applicant's arguments have been fully considered but are not found to be persuasive.

Applicant has submitted declarations in an attempt to overcome the rejection. However, these declarations are found to be unpersuasive. First, the declaration of Dr. Doughty states that pharmaceutical tablets can be formulated by wet or dry methods, and that each of these methods can impart different physical characteristics to the final tablet. This statement affirms the examiner's position that the Johnson formulation may have been made using dry granulation, particularly because, as Applicant admits, both wet and dry granulation techniques are known in the art.

The Affidavits of Drs. Rhodes and Roman again discuss the improvements realized by changing the wet granulation tablet formulation to dry admixing and compressing process. Drs. Rhodes and Roman admit that the pink hue did not appear in every batch using wet granulation. This reiterates the examiner's above point, that using wet granulation or drug granulation, the

formulation may develop a pink hue. (Dr. Doughty declared that the pink hue has only been made less likely, it has not completely disappeared, and Drs. Rhodes and Roman admit that the pink hue did not appear all the time using wet granulation). Applicant has stated that the major improvement in their invention revolves around the alleged pink hue of the prior art, however, it appears that this pink hue can still appear. It is therefore unclear what the claimed improvement is.

Furthermore, the declarations and affidavits continuously discuss the prior art as though it clearly stated that the products were made using wet granulation. As stated before, this is clearly not the case. There has been no evidence provided to show that Johnson used wet granulation. In fact, as stated in the above rejections, it is the position of the examiner that Johnson *was* made using *dry* processes, rather than wet processes as asserted by Applicant. Johnson does not teach, anywhere in his disclosure, that a wet formulation process is employed. Applicant is making a blanket and unsupported statement that all paroxetine formulations, *except their own*, have been made using wet granulation. Absent evidence to support such a strong assertion, the examiner relies on the above rejections. Furthermore, the examiner relies on the teachings in the cited art, which show that dry processes were known and employed at the time of the Johnson reference.

Additionally, there is no evidence that the product disclosed by Johnson possesses the pink hue as suggested by applicant. Therefore, there is nothing in the Johnson reference to back up Applicant's claim that Johnson used wet granulation.

The examiner has some additional comments to set forth regarding the instant claims and the declarations. First, much of the discussion surrounding this prosecution relates to the presence of the "pink hue". As discussed above, Applicant himself admits that the pink hue can

be present in both the wet and dry granulation formulations. Therefore, this does not amount to a showing of unexpected results. Additionally, it would be obvious to one of ordinary skill in the chemical and pharmaceutical arts that a change in color represents a chemical reaction. To those skilled in the pharmaceutical industry, the first and most obvious change would be to remove or add water, depending on the original process used.

Lastly, paragraphs 10-13 of Dr. Roman's declaration are considered misleading. Paragraphs 10 and 11 discuss that the pink hue is a result of n impurity referred to as the "paroxetine catechol." However, in paragraphs 12 and 13, only the removal of water is discussed in attempting to remove the pink hue. Is there something more important involving the presence of this impurity?

Claims 20-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 269 303 to Lassen, in vies of Remington's Pharmaceutical Sciences, either the 15th or the 17th edition.

Lassen discloses a method for treating pain which comprises administering an effective amount of paroxetine or an acceptable salt thereof (abstract). Lassen further teaches that an acceptable salt of paroxetine is paroxetine hydrochloride (p 2, l 14). Lassen also teaches that the medicament can be in tablet form for oral administration (p 2, l 33-36), and may include excipients suitable for oral administration, such as calcium phosphate, magnesium stearate, and sodium starch glycolate (p 2, l 39-44). Lassen also teaches that the formulation will generally contain between 2 and 1000 mg, more preferably between 30 and 500 mg per dosage form (p 3, l 17-20). Lastly, Lassen teaches that the formulation may be obtained by conventional methods of blending, filling, tabletting, or the like (p 2, l 45-46).

Lassen does not specifically teach that dry mixing is employed. However, Lassen can be taken in view of Remington's. Both the Fifteenth Edition and the Seventeenth Edition of Remington's Pharmaceutical Sciences, published in 1975 and 1990, respectively, teach that there are three known processes for making tablets- wet granulation, dry granulation and direct compression. Remington's teaches that there are reasons for choosing one method over another, for instance, wet granulation has a greater number of steps required, as well as increased time and labor. Additionally, wet granulation is unsuccessful with actives which are sensitive to moisture or temperature. On the other hand, dry granulation is useful with actives which are sensitive to moisture and which have sufficient inherent binding or cohesive properties.

It is the position of the examiner that one of ordinary skill in the art would have been motivated to combined the teachings of the above two references. First, Lassen teaches that the formulation may be made by any conventional method known in the art. Second, Lassen does not teach the presence of water, or a different solvent, and instead teaches mixing the components listed in any conventional manner. One skilled in the art would look to a well known pharmaceutical guidebook, such as Remington's, to determine what "conventional methods" entail. As stated above, Remington's teaches three known methods: wet granulation, dry granulation, and direct compression. Therefore, absent evidence to the contrary, one skilled in the art would have been motivated to use any of these well known methods to make the formulation disclosed by Lassen. Furthermore, it would have been obvious to chose the method which would allow the producer to obtain the best possible product, in both appearance and function. The expected result would be a successful pharmaceutical formulation successful in

the treatment of a patient in need thereof. Therefore, this invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Applicant's arguments have been fully considered but are not found to be persuasive. The arguments regarding this rejection are similar to the ones regarding the Johnson rejection, and therefore no additional response to those arguments is deemed necessary.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E Pulliam whose telephone number is 703-308-4710. The examiner can normally be reached on Mon-Thurs 7:30-5:00, Alternate Fri 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3592 for regular communications and 703-305-3592 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

A. Pulliam
Patent Examiner
Tech Center 1600/ AU 1615
November 20, 2003

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